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INTERNATIONAL APPLICATION PUBLISE	HED U	UNDER THE PATENT COOPERATION TREATY (PCT)
(51) International Patent Classification <sup>6</sup> :		(11) International Publication Number: WO 97/08314
C12N 15/12, C07K 14/47, 16/18, C12N 5/12, C12Q 1/68, C12N 5/10, 1/21, G01N 33/53, C12Q 1/00, A61K 38/17, C12N 7/01, C07K 1/22	A3	(43) International Publication Date: 6 March 1997 (06.03.97)
(21) International Application Number: PCT/USS (22) International Filing Date: 23 August 1996 (2		DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).
(30) Priority Data: 08/519,103 25 August 1995 (25.08.95)	ι	Published  With international search report.  Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.
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(54) Title: TELOMERE REPEAT BINDING FACTOR AND DIAGNOSTIC AND THERAPEUTIC USE THEREOF

#### (57) Abstract

The present invention relates to a nucleotide sequence encoding a telomeric protein which binds a repeat region of telomeric sequences, and to the protein encoded thereby. Also included within the invention are expression vectors for the production of the telomeric protein and host cells transformed with the nucleotide sequence. In addition, antibodies, probes and antagonists specific for the telomeric protein are contemplated. Methods of identifying antagonists of the telomeric protein, diagnostic methods of identifying the telomeric protein in a sample, and therapeutic uses of the telomeric protein, particularly in the treatment of aging and cancer, are also contemplated.

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Intern. al Application No PCT/US 96/13652

A. CLASS IPC 6	IFICATION OF SUBJECT MATTER C12N15/12 C07K14/47 C07K16 C12N5/10 C12N1/21 G01N33 C12N7/01 C07K1/22	/18 C12N5/12 /53 C12Q1/00	C12Q1/68 A61K38/17	
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B. FIELDS	S SEARCHED			
IPC 6	C12N C07K C12Q G01N A61K	ication symbols)		
Documenta	tion searched other than minimum documentation to the extent the	nat such documents are included in the	he fields searched	
Electronic	tata base consulted during the international search (name of data	base and, where practical, search ter	ms used)	
C. DOCUN	MENTS CONSIDERED TO BE RELEVANT			
Category *	Citation of document, with indication, where appropriate, of the	ne relevant passages	Relevant to claim No.	
x	PROCEEDINGS OF THE NATIONAL ACA SCIENCES OF USA, vol. 91, no. 19, 13 September 1		1-7,19, 20	
	WASHINGTON US, pages 8861-8865, XP002019942			
	JOHN P. HANISH ET AL.: "Stringent sequence requirements for the formation of			
	human telomeres" cited in the application			
	see page 8861, left-hand column, last paragraph - right-hand column, paragraph 2 see page 8862, left-hand column, paragraph			
	7 see page 8864, left-hand column, last paragraph - right-hand column, paragraph 1			
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X Furt	ther documents are listed in the continuation of box C.	Patent (amily members a	are listed in annex.	
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Name and	mailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL - 2280 HV Rijswijk	Authorized officer		
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2

Internal al Application No PCT/US 96/13652

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MOLECULAR AND CELLULAR BIOLOGY, vol. 12, no. 11, November 1992, pages 4834-4843, XP000610908 ZHONG ZHONG ET AL.: "A mammalian factor that binds telomeric TTAGGG repeats in vitro" cited in the application see abstract see page 4836, left-hand column, paragraph 3 - page 4841, right-hand column, paragraph 1	1-12, 21-24, 31,49, 50,52
X	MOL. CELL. BIOL. (1995), 15(3), 1144-53 CODEN: MCEBD4; ISSN: 0270-7306, 1995, XP000610904 SHENG, HONG ET AL: "Identification and characterization of a putative telomere end- binding protein from Tetrahymena thermophila" see abstract see page 1146, left-hand column, paragraph 1 - right-hand column, paragraph 1 see page 1150, right-hand column, paragraph 2 - page 1152, left-hand column, paragraph 2	1,6,7,21-24
A	EMBO JOURNAL, vol. 11, no. 2, February 1992, EYNSHAM, OXFORD GB, pages 717-724, XP002019943 TITIA DE LANGE: "Human telomeres are attached to the nuclear matrix" see page 717, right-hand column, paragraph 2 - page 718, left-hand column, paragraph 1 see page 719, left-hand column, paragraph 2 - page 720, left-hand column, paragraph 1 see page 721, left-hand column, paragraph 3 - page 722, right-hand column, paragraph 2	1-7,21, 23-25,49
A	NUCLEIC ACIDS RES. (1992), 20(24), 6461-4 CODEN: NARHAD; ISSN: 0305-1048, 1992, XP002019944 MCKAY, STEWART J. ET AL: "hnRNP A2/B1 binds specifically to single stranded vertebrate telomeric repeat TTAGGGn" see the whole document	1-7

Interne 1 Application No PCT/US 96/13652

		PC1/03 90/13032
	nton) DOCUMENTS CONSIDERED TO BE RELEVANT	Relevant to claim No.
Category *	Citation of document, with indication, where appropriate, of the relevant passages	
A	MOL. CELL. BIOL. (1993), 13(7), 4301-10 CODEN: MCEBD4;ISSN: 0270-7306, 1993, XP000610903 ISHIKAWA, FUYUKI ET AL: "Nuclear proteins that bind the pre-mRNA 3' splice site sequence r(UUAG/G) and the human telomeric DNA sequence d(TTAGGG)n" see abstract see page 4302, left-hand column, paragraph 2 - right-hand column, paragraph 1 see page 4302, right-hand column, paragraph 4 - page 4304, left-hand column, paragraph 2 see page 4307, right-hand column, paragraph 2 - page 4309, right-hand column, paragraph 1	
P,X	NUCLEIC ACIDS RES. (1996), 24(7), 1294-303 CODEN: NARHAD;ISSN: 0305-1048, 1996, XP002019946 BILAUD, THOMAS ET AL: "The telobox, a myb-related telomeric DNA binding motif found in proteins from yeast, plants and human" see page 1295, left-hand column, paragraph 2 - right-hand column, paragraph 1 see page 1297, right-hand column, paragraph 3 - page 1302, right-hand column, paragraph 2	1-3,5, 8-13,21
P,X	SCIENCE, vol. 270, 8 December 1995, LANCASTER, PA US, pages 1663-1667, XP002019947 LAURA CHONG ET AL.: "A human telomeric protein" see the whole document	1-25, 31-52
P,X	SEMINARS IN CELL & DEVELOPMENTAL BIOLOGY 7 (1). 1996. 23-29. ISSN: 1084-9521, XP000610905 DE LANGE T: "In search of vertebrate telomeric proteins." see page 26, right-hand column, paragraph 2 - page 27, left-hand column, paragraph 2 see page 28, left-hand column, paragraph 2	1-7, 21-30

2

I national application No.

PCT/US 96/13652

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: 26-29 because they relate to subject matter not required to be searched by this Authority, namely:  Remark: Although these claims are directed to a method of treatment of the human/animal body the search has been carried out and based on the alleged effects of the compound/composition.
Claims Nos.:  because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.